

The Role of Genotyping in TB Prevention and Control Activities

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Early diagnosis and effective treatment of disease, contact tracing, and treatment of infected contacts are the major strategies for limiting the transmission of tuberculosis. Preventing further transmission of the disease is a collective responsibility that requires the efforts of public health officials, health care providers, and laboratories. This is accomplished by finding contacts of infectious patients and ensuring that they are promptly evaluated and, if infected, that they complete a course of therapy for latent TB infection. Genotyping of TB isolates is a relatively new technology that has emerged as an additional tool in TB control and prevention efforts.

How Genotyping Benefits TB Control Programs

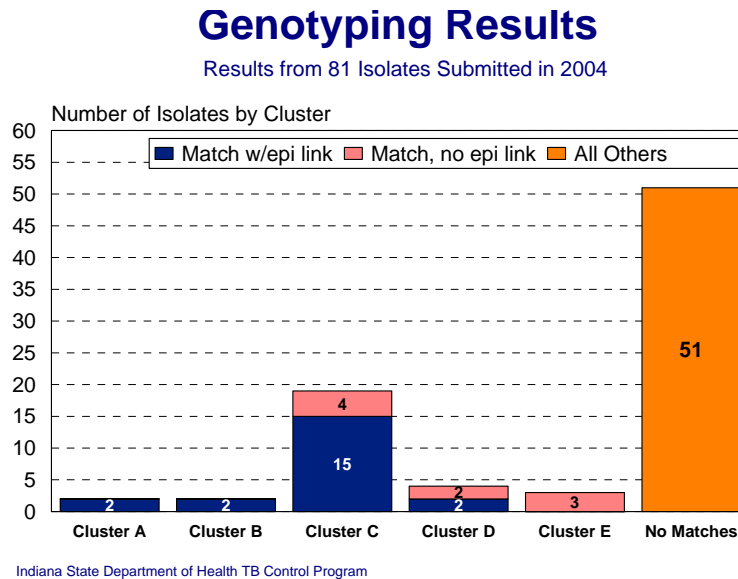
In 2004, the Indiana State Department of Health (ISDH) began to participate in the Centers for Disease Control and Prevention (CDC) Genotyping Program. By helping to identify TB patients who are involved in recent transmission, genotyping will have the following impact:

- Outbreaks can be detected earlier and controlled more rapidly.
- Incorrect TB diagnoses based on false-positive culture results can be identified more easily.
- Unsuspected relationships between cases and new and unusual transmission settings will be discovered.
- Transmission that occurs between patients who reside in different jurisdictions will be detected more readily.
- TB control programs will be able to evaluate completeness of routine contact investigations.

Since the early 1990s, a form of genotyping known as restriction fragment-length polymorphism (RFLP) has been in use. This method analyzes the insertion sequence IS6110, which is found in the genome of all strains of *M. tuberculosis* and *M. bovis*. Genotyping is currently being performed with two relatively new techniques based on the polymerase chain reaction (PCR): spacer oligonucleotide typing (spoligotyping) and mycobacterial interspersed repetitive units (MIRU) analysis.

Genotyping has played a significant role in understanding the transmission patterns of TB cases in several Indiana counties during the last eight years. It has also detected several cases of false positive TB cultures that were the result of laboratory contamination. Figure 1 shows matching genotypes grouped by cluster. Of the 81 isolates submitted this year for which genotype results are available, there were 30 matches grouped into 5 different clusters. Genotypes from the remaining 51 isolates did not match any others.

Figure 1.



How TB Genotyping Helps TB Prevention and Control Practices

When combined with epidemiologic data, TB genotyping results help to distinguish TB patients who are involved in the same chain of recent transmission from patients whose disease is the result of reactivation of a past TB infection. Since TB prevention and control efforts directed at preventing TB transmission (early diagnosis, treatment, and isolation) are fundamentally different from efforts to prevent reactivation (identification and treatment of infected contacts), genotyping offers a powerful tool to help direct the application of these different efforts.

TB genotyping identifies genetic links between *Mycobacterium tuberculosis* isolates from different TB patients. The key to determining if TB patients with matching genotypes are involved in the same chain of recent transmission is to investigate whether the patients share epidemiologic links that can explain where and how the exposure took place. If two patients with TB are known to have been in the same place when one of them was infectious, both are said to share known epidemiologic links. If two patients have isolates with matching genotypes and they also share known epidemiologic links, this provides strong evidence that they are involved in the same chain of recent transmission. In cases where the genotypes match but no epidemiologic links can be established, those patients were possibly involved in the same recent chain of transmission in some way, but a thorough contact investigation and detailed patient interviews should be conducted to determine if the patients share any common risk factors, such as living in the same neighborhood, frequenting the same bars and clubs, or working in the same building. It is also possible that patients whose genotypes match but have no epidemiologic links to one another belong to the same genotyping cluster but were not involved in the same recent transmission. If two or more patients have genotypes that do not match, we can conclude that their TB disease is the result of reaction of an old infection rather than the result of recent transmission.

Genotyping will continue to perform a valuable role as an adjunct to conventional contact investigations and clinical diagnosis for the foreseeable future.

References:

1. Indiana State Department of Health Tuberculosis Information Management System database.
 2. Friedman, Lloyd N. *Tuberculosis: Current Concepts and Treatment*. Boca Raton: CRC Press. 1994.
 3. Driscoll, Jeffery R., et al. "How and Why We Fingerprint Tuberculosis." RT, *The Journal for Respiratory Care Practitioners*, February/March 2001.
 4. Centers for Disease Control and Prevention. *Guide to the Application of Genotyping to Tuberculosis Prevention and Control*, June 2004.
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